Worldwide survey of nutritional practices in pediatric intensive care units

Dorian Kerklaan, MD[1]*, Tom Fivez, MD[2]*, Jessie M. Hulst[3], Dieter Mesotten, MD, PhD[2], Joost van Rosmalen, PhD[4], Nilesh M. Mehta, MD, PhD[5], Greet Van den Berghe, MD, PhD[2], Koen F.M. Joosten MD, PhD[1], Sascha C.A.T. Verbruggen, MD, PHD[1]

* contributed equally

[1]Pediatric Intensive Care Unit, Erasmus MC - Sophia Children's Hospital, Rotterdam, the Netherlands

[2]Clinical Department and Laboratory of Intensive Care Medicine, Academic Division Cellular and Molecular Medicine, KU Leuven University and Hospital, Leuven, Belgium

[3]Department of Pediatric Gastroenterology, Erasmus MC - Sophia Children's Hospital, Rotterdam, The Netherlands.

[4]Department of Biostatistics, Erasmus MC, Rotterdam, The Netherlands

[5]Boston Children's Hospital, Harvard Medical School, Boston, U.S.A.

For information regarding this article:
Sascha Verbruggen, MD, PhD
Department Pediatric Intensive Care Unit, Erasmus MC – Sophia Children's Hospital, Rotterdam, P.O. Box 2060, 3000 CB Rotterdam, The Netherlands. Email: s.verbruggen@erasmusmc.nl

This research was partially supported by grants from IWT-TBM 110685, Fonds NutsOhra and the Erasmus –Trustfonds. DM holds a senior clinical investigator fellowship from the FWO research foundation Flanders Belgium. For the remaining authors none were declared.

Abstract (max 300 words, nu 287)

Objective

To assess current nutritional practices in critically ill children worldwide.

Design

A two-part online, international survey. The first part, the *survey,* was composed of 59 questions regarding nutritional strategies and protocols (July-November 2013). The second part surveyed the *point-prevalence* of nutritional data of patients present in a subgroup of the responding PICUs (May-September 2014).

Setting

Members of the World Federation of Pediatric Intensive and Critical Care Societies were asked to fill out the survey.

Subjects

Pediatric critical care providers.

Interventions

Survey.

Measurements and Main Results

We analyzed 189 responses from 156 PICUs in 52 countries (*survey*). We received nutritional data on 295 patients from 41 of these 156 responding PICUs in 27 countries (*point-prevalence*). According to the *survey*, nutritional protocols and support teams were available in 52% and 57% of the PICUs, respectively. Various equations were in use to estimate energy requirements; only in 14% of PICUs indirect calorimetry was used. Nutritional targets for macronutrients varied widely. Enteral nutrition (EN) would be started early (within 24 hours of admission) in 60% of PICUs; preferably by the gastric route (88%). In patients intolerant to EN, parenteral nutrition (PN) would be started within 48 hours in 55% of PICUs. Overall, in 72% of PICUs supplemental PN would be used if EN failed to meet at least 50% of energy delivery goal.

Several differences between the intended (*survey*) and the actual (*point prevalence*) nutritional practices were found in the responding PICUs, predominantly overestimating the ability to adequately feed patients.

Conclusion

Nutritional practices vary widely between PICUs worldwide. There are significant differences in macronutrient goals, estimating energy requirements, timing of nutrient delivery, and threshold for supplemental PN. Uniform consensus-based nutrition practices, preferably guided by evidence, are desirable in the PICU.

Keywords (max 6): Pediatric; intensive care units; nutritional support; parenteral nutrition; enteral nutrition; questionnaires

Introduction

Nutritional support affects recovery and outcome in critically ill children [1-3]. Although undernutrition has long been the primary focus [1, 4, 5], overfeeding in Pediatric Intensive Care Units (PICUs) is also prevalent and associated with greater morbidity [6-8]. Despite its clinical relevance, there is a scarcity of high-level evidence on various aspects of nutritional support in critically ill children [9, 10]. With grade C as the maximum level of evidence, the available guidelines for nutrition support in critically ill children are based on insufficient data to make evidence-based recommendations.

As a result there are no clear guidelines for nutritional support in the PICU. Consensus-based guidelines provided by expert committees (American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.), European Society for Clinical Nutrition and Metabolism (ESPEN) and the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN)) are based on expert opinion and extrapolations from studies in adults or non-critically ill children [11, 12]. This potentially allows wide variations in current nutritional support practice for pediatric patients in ICUs in several European countries as shown in previous studies [13, 14]. The variability in timing, amount and composition of nutrition would inevitably result in malnutrition (i.e. underfeeding and overfeeding), which could potentially impact the clinical outcome of critically ill children. Thereby it could be affecting health care expenses [15].

The purpose of our study was to assess the current nutritional practice in PICUs across the world. We hypothesized that the limited guidelines available have not been universally implemented, and that current practice is heterogeneous and mostly physician based. Since the guidelines at least agree on the importance of enteral nutrition (EN) [11, 16, 17], we expect no significant differences in this practice between PICUs. Other factors, such as assessment of energy requirements or use of parenteral nutrition (PN), are more likely to vary between countries and hospitals given the weak recommendations.

To quantify the variations in clinical practice, we distributed a two-part online survey to PICUs across the world. The first part of the *survey* was composed of questions on various aspects of local nutritional practice. The second part was a *point-prevalence* survey on nutritional data collected in all patients present in a PICU on a single day in a subgroup of the responding PICUs. Answers were analyzed, correlated with PICU characteristics and differences between the intended (*survey*) and the actual (*point prevalence*) nutritional practices were determined.

Material and Methods

The local Institutional Review Board waived the need for consent.

The first part of this cross-sectional *survey* was conducted between July and November 2013. The online questionnaire (https://erasmusmcsurvey.erasmusmc.nl/picu/), was composed of 59 questions regarding local nutritional protocols and strategies, and provided in English, French, Spanish and Chinese. The second part (https://erasmusmcsurvey.erasmusmc.nl/sophia-ick/): the *point-prevalence*, conducted between May and September 2014, involved data collection on nutritional practices and nutritional intake for the preceding 24 hours in all patients present in the participating PICUs. Both questionnaires are included as online digital supplement to this article.

Testing of the clarity, relevance and clinical sensibility of the questionnaire was performed by independent clinicians in three different centers (Sophia Children's Hospital-Erasmus MC, Rotterdam, the Netherlands; University Hospital of Leuven, Belgium; and the Boston Children's Hospital, U.S.A.). Data from this test were not included in the final analysis and survey results.

An invitation to the *survey* was electronically distributed to members of the World Federation of Pediatric Intensive and Critical Care Societies (WFPICCS) and to specific members of the European Society of Paediatric and Neonatal Intensive Care (ESPNIC) and Society of Critical Care Medicine (SCCM) involved in nutritional management. Due to incomplete data registration, the number of PICUs represented by the WFPICCS database is unknown. A reminder was sent 2 months after the first invitation, and invitations to participate were also send through the newsletter of both the ESPNIC and WFPICCS and the WFPICCS homepage and LinkedIn group. Respondents that provided their contact information in the *survey,* were approached to participate in the *point-prevalence*.

If more than one questionnaire was returned from a single PICU, the answers were weighted by the inverse of the number of completed questionnaires per center, in order to process conflicting statements within a single institution without disrupting the weight of the answers per PICU. Countries were classified by income according to The World Bank income groups [18]. Individual questions were stratified by continent, income of country, number of PICU beds, admissions per year and percentage of ventilated patients.

Statistical analysis was performed using IBM SPSS statistics 21 for Windows (IBM, Chicago IL, USA). Descriptive statistics were used to compare differences in respondent characteristics and survey responses. Nutritional data obtained in the *point-prevalence,* were compared to the *survey* results for each participating center. Logistic regression, ordinal or multinomial, depending on the type of outcome, was used to identify the relation between the answers provided and the characteristics of the different PICUs. To correct for cluster effects due to multiple returned questionnaires per PICU, generalized estimating equations were used in conjunction with robust standard error estimates (Huber sandwich estimator). All statistical tests were two-sided and statistical significance was defined as a P-value < 0.05.

This trial was registered in the Dutch Trial Register (NTR) at number 4093 (www.trialregister.nl).

Results

Response

After distribution of the first part of the *survey* a total of 251 questionnaires were received. Fifty-two questionnaires were removed because of missing essential data. Of the remaining 199 questionnaires, 10 were duplicate replies by the same respondent and therefore deleted. 189 questionnaires were analyzed, representing 156 PICUs in 52 countries and 6 continents as shown in Figure 1.

For the *point-prevalence* we collected nutritional data on 295 patients in total, from 41 of the responding PICUs (26%) from 27 countries on 6 continents with a median input of 5 patients (IQR 2-9) per PICU. Characteristics of responding PICUs for the *point-prevalence* were similar compared to the overall *survey* respondents (Table 1).

PICU and patient demographics

The responding PICUs in the first part of the *survey* represented approximately 90,000 admissions per year with a mean annual admission rate of 612 (IQR 296-793) patients. Fifty-two percent of PICUs were located in North-America and Europe. Fourteen percent of PICUs were situated in low or lower middle income countries and 86% of PICUs were multidisciplinary. All PICU demographics are shown in Table 1.

Of the 295 patients included in the *point-prevalence*, 60% was male and 58% younger than 1 year of age. Median length of stay (LOS) at moment of data collection was 6 days (IQR 2-15), with 40% of the patients being admitted for more than 7 days. Median weight was 7 kg (IQR 4-16) and 46% of the children were mechanically ventilated.

Nutritional support

According to the first part of the *survey*, a nutritional protocol was present in 52% of PICUs; protocol characteristics are shown in Table 2. A Nutrition Support Team (NST) was available in 57% of the PICUs and 51% of the teams visited the ICU daily. The composition of an NST differed; it consisted mostly of dieticians (88%) and pediatric intensivists (51%).

In the *point prevalence*, median caloric intake did not differ between PICUs with an NST (76 kcal/kg/day), nutritional protocol (76 kcal/kg/day) or both (64 kcal/kg/day) or in absence of both an NST and protocol (58 kcal/kg/day) (p=0.18) in children fed by EN exclusively (n=129). There was also no difference in the proportion of children receiving EN in PICUs with and without an NST and/or protocol.

Nutritional requirements

To predict energy expenditure (EE) different equations were used according to the first part of the *survey*, mainly those published by Schofield (25%) and the WHO (25%), but also the Harris-Benedict equation (17%) [19-21]. Twenty-four percent of respondents did not know which equation was used to calculate EE in their unit. Indirect calorimetry (IC) to measure EE was used in only 14% of the PICUs .

Protein targets recommended by the A.S.P.E.N. and ESPEN/ESPGHAN guidelines were respectively followed in 31% and 36% of PICUs when selecting a guideline-recommended-protein targets that was closest to the local target protein intake in the PICU. This reflects an age-dependent range of 0.9 to 3 g protein/kg/day [11, 12]. Lipid targets ranged from < 1.5 to > 3.5 g/kg/day; where the range of 1.5 to 2.5 g/kg/day was predominantly used (41%). Sixteen percent and 7.9% of the respondents did not know what their protein and lipid targets were, respectively.

In the *point-prevalence*, median caloric intake was 66 kcal/kg/day (IQR 49-96) for children on EN exclusively (n=129); intake per kg of weight decreased significantly with age as expected ($p<0.001$, Fig. 2). In 31% of the children the caloric intake was lower than basal metabolic rate calculated by the weight-based Schofield equation; for the WHO equation this was 27%. Median protein intake was 1.8 g/kg/day (IQR 1.2-2.6); only 34% of the children met the intended target protein intake of their PICU as mentioned in the *survey*.

Timing and route of nutrition

In the first part of the *survey*, an early start (within 24 hours after admission) of enteral nutrition (EN) was mentioned for 60% of PICUs; in 31% EN would even be started within 12 hours (Fig. 3). Fifty-nine percent of the respondents had the perception that they were able to feed patients exclusively by enteral route within 3 days post-admission. The gastric route was preferred for enteral nutrition in ventilated (67% of PICUs) and non-ventilated patients (88%). Pro-kinetics were prescribed when a patient was not tolerating feeds in 70% of PICUs.

Early parenteral nutrition (PN) was started within 48 hours after admission in 55% of PICUs, while only in 3.5% of PICUs there would be a waiting time of at least 7 days to start PN (Fig. 3).

When EN was insufficient, respondents from 18% of the PICUs would always supplement PN, whereas in 7.5% additional PN would never be utilized. Seventy-two percent supplemented PN if EN failed to meet 50% of target calories; 24% if EN failed to meet 80%. PN was stopped in 64% of PICUs when EN covered > 80% of the nutritional targets.

At the moment of our *point-prevalence* 73% of the children received EN (n=216), predominantly by gastric tube (70%). There was no difference in caloric intake (p=0.82) or in pro-kinetics use (p=0.47) between children fed by gastric or post-pyloric route. Forty-two percent of children with a length of stay < 24 hours (n=43) were already receiving EN and in children with a length of stay of 2 days or more (n= 253) EN in some form was provided in 78%. Twenty-one percent of all children received PN in some form and 10% received a combination of EN and PN; both groups at a median length of stay of 6.5 days. The *point-prevalence* showed that the ability to administer exclusive EN was overestimated; 40% of children (n=74) present during the point-prevalence achieved exclusive EN later than perceived by the respondent from the first part of the survey.

Glucose and glycemic control

In the first part of the *survey*, target intake of glucose during the first 12-24 hours of admission varied between < 2 to > 6 mg/kg/min for different weight ranges (Fig. 4). In 62% of the PICUs a protocol for some form of "tight" glycemic control was available. Target blood glucoses were defined as < 10 mmol/L (180 mg/dL) in 54%, and < 8 mmol/L in 23%. Tight glucose control (2.8-4.4 mmol/L or 50-80 mg/dl < 1 year or 3.9-5.5 mmol/L or 70-100 mg/dl 1-16 years) as reported by Vlasselaers et al [22] was practiced in 10% of PICUs.

At the time of the *point-prevalence*, 20 children, median weight 8.1 kg, received exclusive glucose infusion while being admitted < 24 hours; median glucose intake was 1.7 mg/kg/min (IQR 0.3-2.3). Seventy-five percent received less glucose than their target glucose intake (Fig. 4).

Insulin was administered in 32 children (11%); 24 children on insulin were admitted to a PICU with a glucose target < 10 mmol/L (180 mg/dL), 5 to a PICU that practiced tight glucose control as reported by Vlasselaers et al [22].

Administration of parenteral lipids and protein

According to the first part of the *survey*, lipids were supplied in different compositions (Table 3) and in 44% of PICUs a step-up protocol was used that would start at 50% of the maximal dose. Lipid intake was decreased when triglycerides were 3.5-5.5 mmol/L (in 69%) and stopped when triglycerides exceeded 5 mmol/L (in 70%). In case of sepsis, lipid administration was decreased or stopped in 50% of PICUs. Reasons provided to decrease or stop the intake of protein were kidney failure (65%) and urea levels >15 mmol/L (75%).

Geographic and socioeconomic differences

An NST was more often available in PICUs situated in North America (p=0.014), South America (p=0.005) and Oceania (p=0.013) than in Europe and in PICUs with more admissions per year (p=0.029). A higher percentage of nutritional protocols (p=0.006) and support teams (p<0.001) were available in high-income countries than low-middle ones. As expected, protein targets in North American PICUs were more often based on A.S.P.E.N. (p=0.011) and less frequently on ESPEN/ESPGHAN guidelines (p<0.001) than protein targets in Europe. EN was started earlier in PICUs in high-income countries (81% within 24 hours) than in lower-middle-income countries (74% within 24 hours, p=0.012). PN was started later in PICUs in North America (median 2-4 days, p=0.02) and Asia (median 2-4 days, p=0.06) than in PICUs in Europe (median < 48 hours) in a child intolerable to enteral feeds. An overview of the adjusted Odds Ratios per continent is provided in Table 1 of the online supplement.

Discussion

Nutritional practices vary greatly between PICUs worldwide. Several aspects of nutritional support differ significantly; such as macronutrient goals, preferred route and timing of nutrient delivery, estimation of energy requirements, and the threshold for supplemental PN use. These differences were apparent between PICUs in general, and also between geographic and socioeconomic regions. Many of these areas currently lack evidence. In addition, applied nutritional practice deviates from local protocols or strategies on multiple occasions as shown in our comparison of survey and point-prevalence results per PICU, increasing the variation of clinical nutritional practice even more.

Globally, guidelines for nutritional support are released by nutritional organizations. The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) and European Society for Clinical Nutrition and Metabolism combined with the European Society for Paediatric

Gastroenterology Hepatology and Nutrition (ESPEN/ESPGHAN) provide specific guidelines for nutrition in critically ill children. However, they do not advise on every aspect of nutritional support. Agreements and differences between these guidelines and current practice, as shown by our survey, are summarized in Table 4.

Overall, the most striking similarity between guidelines and local implementation, is the preference for enteral nutrition and its early initiation in critically ill children.

A specialized nutrition support team and aggressive feeding protocols are recommended by the A.S.P.E.N guidelines for critically ill children (grade E) [11]. While availability of a protocol is associated with a lower prevalence of hospital-acquired infections [3], the implementation of a support team or an enteral nutrition algorithm has been reported to lead to an increase in EN use and energy intake, but with inconclusive effect on patient outcome [23-25]. Our *survey* showed that a nutritional protocol and/or nutritional support team were available to most PICUs, but we found no significant effect on intake and use of EN in the *point prevalence*.

The ESPEN/ESPGHAN guidelines prefer the measurement of REE to the use of equations. The A.S.P.E.N. guidelines recommend targeted use of indirect calorimetry (IC) in a select group of patients with suspected metabolic alterations or malnutrition if IC is available (Table 4). Both state that in the absence of IC, reasonable values can also be derived from formulas, e.g. Schofield, but only when applied <u>without</u> the use of universal correction factors (stress factors) (grade D) [12]. Several other sources state that nutritional therapy should be targeted on energy expenditure (EE) throughout the course of illness [26-28]. However, due to the limited availability and practice of indirect calorimetry [13, 29], and due also to inaccurate predictive equations [27, 28, 30-33], it is difficult to assess REE in critically ill children. Use of the WHO and Schofield equations, the equations most commonly used to determine requirements, may lead to underfeeding and overfeeding thereby impacting morbidity and mortality [3, 6, 34]. We confirmed the finding of previous studies [13] that indirect calorimetry to measure EE is used in a small minority of PICUs; in 14% of PICUs worldwide and 20% of PICUs in Europe. In contrast with both guidelines, energy needs were calculated <u>with</u> use of correction factors in the majority of PICUs in absence of IC. Remarkably, in the *point-prevalence* 1/3 of the children on exclusive EN received less calories than BMR calculated by the Schofield or WHO formula.

Timing of nutrition is not widely covered by the pediatric ESPEN/ESPGHAN and A.S.P.E.N. guidelines (Table 4). The adult guidelines from the same societies agree on the importance of early enteral nutrition but contain contradictory recommendations regarding parenteral nutrition [16, 17, 35]. The importance and benefits of early enteral nutrition are generally accepted in previous studies in adults and children [1, 36-43], and in critically ill children a higher intake by enteral route is associated with a lower 60-days mortality [3]. In our *survey* as well as in the *point-prevalence* EN and PN were both initiated early; within 24 and 48 hours respectively. Overall, characteristics of EN support were quite similar between PICUs. The difference in PN initiation time between Europe and North America could reflect the contradictory recommendations in adult guidelines in these regions, which agree on the importance of early EN but not on the time at which PN should be started [17, 35, 44-46]. The optimal timing and dose of PN is still under debate, despite recent large randomized trials in critically ill adults [47-50].

Post-pyloric feeding may be considered as route of EN in children at high risk of aspiration, but guidelines fail to recommend an appropriate site for enteral feeding. Although post-pyloric feeding might improve caloric intake [51], most patients evaluated in our *survey* and *point-prevalence* were fed by the gastric route with no different intake than children fed post-pyloric (*point-prevalence)*. The time to feed patients exclusively by the enteral route was short; 59% of respondents thought their PICU was able to feed their patients within 3 days, but overestimated. Only 60% of the patients of the *point-prevalence* were actually on exclusive EN within the time frame mentioned in the *survey*. Also prospective data from PICUs on enteral nutrition show that only 38-86% of energy goals were administered via this route [8, 52].

The glucose targets in the ESPEN/ESPGHAN pediatric guidelines are supported by limited evidence, where the A.S.P.E.N guidelines do not provide recommendations on macronutrient intake due to insufficient data. In our *survey* glucose intake targets during the first 12-24 hours tended to range between 2-6 mg/kg/min and decreased with increasing weight. The upper limit of glucose intake for hospitalized children provided in the ESPEN/ESPGHAN guideline (5 mg/kg/min in critically ill children, based on the maximal oxidation rate [53]) was exceeded by more than 7% of PICUs. Additionally, our *point prevalence* showed that in 75% of the patients glucose intake differed from the glucose targets mentioned in the first part of the survey. However, we should be very careful to draw conclusions from that number, because only 20 children received glucose infusion exclusively during the first 24 hours of admission. Target blood glucose levels varied between tight control as reported by Vlasselaers et al [22] and a target glucose < 10 mmol/L. This discrepancy in definitions and implementation in glucose management has been highlighted before [54-57]. Glucose management is known to impact outcome and recovery, but uncertainties about risks and benefits remain [22, 58, 59].

The strength of our study is the fact that we surveyed the local nutritional strategies as well as their implementation in clinical practice, and, to our knowledge, that this is the largest study on nutritional support and practice in PICUs so far in terms of number of responses and international distribution. Furthermore it is the only study to cover 6 continents and both low and high-income countries.

However, no response rate can be calculated since it is not known how many PICUs are represented by the WFPICCS database. Based on the number of PICUs in countries joined in the WFPICCS, identified in the literature (at least 969 PICUs in total), our data from 156 PICUs represent a small proportion of all PICUs worldwide. Our study may also be limited by the possibility that non-respondents of this survey were less interested in nutritional practices leading to a selection bias and possible distorted reflection of nutritional practices. On the other hand, this selection-bias may enforce our conclusion, if even in the nutrition-minded respondents, adherence to available guidelines is limited. Finally, many of the questions required an unambiguous answer, which may have been difficult due to the varied nature of the PICU population. We therefore asked our respondents to provide the most applicable answer.

Nevertheless, our survey clearly demonstrates the international variety of nutritional practice in critically ill children and the differences due to the limited available guidelines; especially on macronutrient administration and calculation of energy targets.

Conclusion

In terms of requirements, timing and route, nutritional practices among critically ill children vary greatly between PICUs worldwide. Even the limited available guidelines are not consistently followed and high-level evidence is urgently needed. The potential impact of the lack of uniform nutritional practices on outcome highlights the need for evidence based guidelines that are implemented consistently.

Acknowledgements

We would like to thank the WFPICCS for their support of this survey. We are also very grateful to all respondents and PICUs for their participation and especially the PICUs that participated in the point-prevalence: Akdeniz University Hospital (Turkey), Astrid Lindgren Children's Hospital – Karolinska University Hospital (Sweden), Beatrix Children's Hospital – University Medical Center Groningen (The Netherlands), Children’s Hospital Vittore Buzzi - Milano(Italy), Clinica Las Condes (Chile), University Children's Hospital Münster (Germany), Dokuz Eylul University (Turkey), Emma Children's Hospital –Academic Medical Center Amsterdam (The Netherlands), Sophia Children’s Hospital – Erasmus MC (The Netherlands), Fundacion Hispanoamericana (Colombia), Government Medical College and Hospital Calicut (India), Grey's Hospital (South-Africa), Haunersche Kinderklinik University Children’s Hospital Munich (Germany), Hôpital d'Enfants de Tunis (Tunisia), Hôpital Femme Mere Enfant (France), Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo (Brazil), Hospital Dr. Guillermo Rawson (Argentina), Hospital for Sick Children (Canada), Hospital General Universitario Gregorio Marañón (Spain), Hospital Israelita Albert Einstein (Brazil), Hospital Nacional Profesor Alejandro Posadas (Argentina), Hospital Pediatrico de Coimbra (Portugal), Hospital Universitario Fundación Favaloro (Argentina), Hospital nacional de Niños (Costa Rica), KK Women's and Children's Hospital (Singapore), Maastricht University Medical Center (The Netherlands), Pediatric Cardiac Center, National Institute of Cardiovascular Diseases (Slovakia), Princess Margaret Hospital for Children (Australia), Queen Mary Hospital (Hong Kong), Shanghai Jiaotong University Affiliated Shanghai Children (China), Shiraz University of Medical Sciences (Iran), Spedali Civili Brescia (Italy), Tampere University Hospital (Finland), Teaching Hospital Karapitiya, Galle (Sri Lanka), The Childrens Hospital Westmead (Australia), Trakya University (Turkey), Unicamp (Brazil), University of Leicester (United Kingdom), UZ Leuven (Belgium), Victoria General Hospital (Canada)

References

1. Briassoulis G, Zavras N, Hatzis T: **Malnutrition, nutritional indices, and early enteral feeding in critically ill children**. *Nutrition* 2001, **17**(7-8):548-557.
2. Pollack MM, Ruttimann UE, Wiley JS: **Nutritional depletions in critically ill children: associations with physiologic instability and increased quantity of care**. *JPEN J Parenter Enteral Nutr* 1985, **9**(3):309-313.
3. Mehta NM, Bechard LJ, Cahill N, Wang M, Day A, Duggan CP, Heyland DK: **Nutritional practices and their relationship to clinical outcomes in critically ill children--an international multicenter cohort study***. *Crit Care Med* 2012, **40**(7):2204-2211.
4. Scrimshaw NS, SanGiovanni JP: **Synergism of nutrition, infection, and immunity: an overview**. *Am J Clin Nutr* 1997, **66**(2):464S-477S.
5. de Souza Menezes F, Leite HP, Koch Nogueira PC: **Malnutrition as an independent predictor of clinical outcome in critically ill children**. *Nutrition* 2012, **28**(3):267-270.
6. Chwals WJ: **Overfeeding the critically ill child: fact or fantasy?** *New Horiz* 1994, **2**(2):147-155.
7. MacIntyre NR, Cook DJ, Ely EW, Jr., Epstein SK, Fink JB, Heffner JE, Hess D, Hubmayer RD, Scheinhorn DJ, American College of Chest P *et al*: **Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine**. *Chest* 2001, **120**(6 Suppl):375S-395S.
8. Mehta NM, Bechard LJ, Dolan M, Ariagno K, Jiang H, Duggan C: **Energy imbalance and the risk of overfeeding in critically ill children**. *Pediatr Crit Care Med* 2011, **12**(4):398-405.
9. Cohen E, Uleryk E, Jasuja M, Parkin PC: **An absence of pediatric randomized controlled trials in general medical journals, 1985-2004**. *J Clin Epidemiol* 2007, **60**(2):118-123.
10. Joffe A, Anton N, Lequier L, Vandermeer B, Tjosvold L, Larsen B, Hartling L: **Nutritional support for critically ill children**. *Cochrane Database Syst Rev* 2009(2):CD005144.
11. Mehta NM, Compher C, Directors ASPENBo: **A.S.P.E.N. Clinical Guidelines: nutrition support of the critically ill child**. *JPEN J Parenter Enteral Nutr* 2009, **33**(3):260-276.
12. Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R, Parenteral Nutrition Guidelines Working G, European Society for Clinical N, Metabolism, European Society of Paediatric Gastroenterology H, Nutrition *et al*: **1. Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR)**. *J Pediatr Gastroenterol Nutr* 2005, **41 Suppl 2**:S1-87.
13. van der Kuip M, Oosterveld MJ, van Bokhorst-de van der Schueren MA, de Meer K, Lafeber HN, Gemke RJ: **Nutritional support in 111 pediatric intensive care units: a European survey**. *Intensive Care Med* 2004, **30**(9):1807-1813.
14. Sharifi MN, Walton A, Chakrabarty G, Rahman T, Neild P, Poullis A: **Nutrition support in intensive care units in England: a snapshot of present practice**. *Br J Nutr* 2011, **106**(8):1240-1244.
15. Correia MI, Waitzberg DL: **The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis**. *Clin Nutr* 2003, **22**(3):235-239.
16. Kreymann KG, Berger MM, Deutz NE, Hiesmayr M, Jolliet P, Kazandjiev G, Nitenberg G, van den Berghe G, Wernerman J, Dgem *et al*: **ESPEN Guidelines on Enteral Nutrition: Intensive care**. *Clin Nutr* 2006, **25**(2):210-223.

17. McClave SA, Martindale RG, Vanek VW, McCarthy M, Roberts P, Taylor B, Ochoa JB, Napolitano L, Cresci G, Directors ASPENBo *et al*: **Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)**. *JPEN J Parenter Enteral Nutr* 2009, **33**(3):277-316.
18. The World Bank: **Country classifications - country and lending groups**. In.: The World Bank; 2014.
19. Schofield WN: **Predicting basal metabolic rate, new standards and review of previous work**. *Hum Nutr Clin Nutr* 1985, **39 Suppl 1**:5-41.
20. **Energy and protein requirements. Report of a joint FAO/WHO/UNU Expert Consultation**. *World Health Organ Tech Rep Ser* 1985, **724**:1-206.
21. Harris JA, Benedict FG: **A Biometric Study of Human Basal Metabolism**. *Proc Natl Acad Sci U S A* 1918, **4**(12):370-373.
22. Vlasselaers D, Milants I, Desmet L, Wouters PJ, Vanhorebeek I, van den Heuvel I, Mesotten D, Casaer MP, Meyfroidt G, Ingels C *et al*: **Intensive insulin therapy for patients in paediatric intensive care: a prospective, randomised controlled study**. *Lancet* 2009, **373**(9663):547-556.
23. Meyer R, Harrison S, Sargent S, Ramnarayan P, Habibi P, Labadarios D: **The impact of enteral feeding protocols on nutritional support in critically ill children**. *J Hum Nutr Diet* 2009, **22**(5):428-436.
24. Hamilton S, McAleer DM, Ariagno K, Barrett M, Stenquist N, Duggan CP, Mehta NM: **A stepwise enteral nutrition algorithm for critically ill children helps achieve nutrient delivery goals***. *Pediatr Crit Care Med* 2014, **15**(7):583-589.
25. Gurgueira GL, Leite HP, Taddei JA, de Carvalho WB: **Outcomes in a pediatric intensive care unit before and after the implementation of a nutrition support team**. *JPEN J Parenter Enteral Nutr* 2005, **29**(3):176-185.
26. White MS, Shepherd RW, McEniery JA: **Energy expenditure measurements in ventilated critically ill children: within- and between-day variability**. *JPEN J Parenter Enteral Nutr* 1999, **23**(5):300-304.
27. Vazquez Martinez JL, Martinez-Romillo PD, Diez Sebastian J, Ruza Tarrio F: **Predicted versus measured energy expenditure by continuous, online indirect calorimetry in ventilated, critically ill children during the early postinjury period**. *Pediatr Crit Care Med* 2004, **5**(1):19-27.
28. Framson CM, LeLeiko NS, Dallal GE, Roubenoff R, Snelling LK, Dwyer JT: **Energy expenditure in critically ill children**. *Pediatr Crit Care Med* 2007, **8**(3):264-267.
29. Smallwood CD, Mehta NM: **Accuracy of abbreviated indirect calorimetry protocols for energy expenditure measurement in critically ill children**. *JPEN J Parenter Enteral Nutr* 2012, **36**(6):693-699.
30. Taylor RM, Cheeseman P, Preedy V, Baker AJ, Grimble G: **Can energy expenditure be predicted in critically ill children?** *Pediatr Crit Care Med* 2003, **4**(2):176-180.
31. Meyer R, Kulinskaya E, Briassoulis G, Taylor RM, Cooper M, Pathan N, Habibi P: **The challenge of developing a new predictive formula to estimate energy requirements in ventilated critically ill children**. *Nutr Clin Pract* 2012, **27**(5):669-676.
32. Coss-Bu JA, Jefferson LS, Walding D, David Y, Smith EO, Klish WJ: **Resting energy expenditure in children in a pediatric intensive care unit: comparison of Harris-Benedict and Talbot predictions with indirect calorimetry values**. *Am J Clin Nutr* 1998, **67**(1):74-80.
33. Briassoulis G, Venkataraman S, Thompson AE: **Energy expenditure in critically ill children**. *Crit Care Med* 2000, **28**(4):1166-1172.

34. Askanazi J, Rosenbaum SH, Hyman AI, Silverberg PA, Milic-Emili J, Kinney JM: **Respiratory changes induced by the large glucose loads of total parenteral nutrition**. *Jama* 1980, **243**(14):1444-1447.
35. Singer P, Berger MM, Van den Berghe G, Biolo G, Calder P, Forbes A, Griffiths R, Kreyman G, Leverve X, Pichard C *et al*: **ESPEN Guidelines on Parenteral Nutrition: intensive care**. *Clin Nutr* 2009, **28**(4):387-400.
36. Elke G, Wang M, Weiler N, Day AG, Heyland DK: **Close to recommended caloric and protein intake by enteral nutrition is associated with better clinical outcome of critically ill septic patients: secondary analysis of a large international nutrition database**. *Crit Care* 2014, **18**(1):R29.
37. McClave SA, Martindale RG, Rice TW, Heyland DK: **Feeding the Critically Ill Patient**. *Crit Care Med* 2014.
38. Mehta NM: **Feeding the Gut During Critical Illness--It Is About Time**. *JPEN J Parenter Enteral Nutr* 2014.
39. Mikhailov TA, Kuhn EM, Manzi J, Christensen M, Collins M, Brown AM, Dechert R, Scanlon MC, Wakeham MK, Goday PS: **Early Enteral Nutrition Is Associated With Lower Mortality in Critically Ill Children**. *JPEN J Parenter Enteral Nutr* 2014.
40. Gramlich L, Kichian K, Pinilla J, Rodych NJ, Dhaliwal R, Heyland DK: **Does enteral nutrition compared to parenteral nutrition result in better outcomes in critically ill adult patients? A systematic review of the literature**. *Nutrition* 2004, **20**(10):843-848.
41. Khorasani EN, Mansouri F: **Effect of early enteral nutrition on morbidity and mortality in children with burns**. *Burns* 2010, **36**(7):1067-1071.
42. Doig GS, Heighes PT, Simpson F, Sweetman EA: **Early enteral nutrition reduces mortality in trauma patients requiring intensive care: a meta-analysis of randomised controlled trials**. *Injury* 2011, **42**(1):50-56.
43. Doig GS, Heighes PT, Simpson F, Sweetman EA, Davies AR: **Early enteral nutrition, provided within 24 h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomised controlled trials**. *Intensive Care Med* 2009, **35**(12):2018-2027.
44. Martindale RG, McClave SA, Vanek VW, McCarthy M, Roberts P, Taylor B, Ochoa JB, Napolitano L, Cresci G, American College of Critical Care M *et al*: **Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition: Executive Summary**. *Crit Care Med* 2009, **37**(5):1757-1761.
45. Heyland DK, Dhaliwal R, Drover JW, Gramlich L, Dodek P, Canadian Critical Care Clinical Practice Guidelines C: **Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients**. *JPEN J Parenter Enteral Nutr* 2003, **27**(5):355-373.
46. Halpern SD, Becker D, Curtis JR, Fowler R, Hyzy R, Kaplan LJ, Rawat N, Sessler CN, Wunsch H, Kahn JM *et al*: **An official american thoracic society/american association of critical-care nurses/american college of chest physicians/society of critical care medicine policy statement: the choosing wisely(R) top 5 list in critical care medicine**. *Am J Respir Crit Care Med* 2014, **190**(7):818-826.
47. Harvey SE, Parrott F, Harrison DA, Bear DE, Segaran E, Beale R, Bellingan G, Leonard R, Mythen MG, Rowan KM *et al*: **Trial of the route of early nutritional support in critically ill adults**. *N Engl J Med* 2014, **371**(18):1673-1684.
48. Casaer MP, Mesotten D, Hermans G, Wouters PJ, Schetz M, Meyfroidt G, Van Cromphaut S, Ingels C, Meersseman P, Muller J *et al*: **Early versus late parenteral nutrition in critically ill adults**. *N Engl J Med* 2011, **365**(6):506-517.

49. Heidegger CP, Berger MM, Graf S, Zingg W, Darmon P, Costanza MC, Thibault R, Pichard C: **Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial**. *Lancet* 2013, **381**(9864):385-393.
50. Doig GS, Simpson F, Sweetman EA, Finfer SR, Cooper DJ, Heighes PT, Davies AR, O'Leary M, Solano T, Peake S *et al*: **Early parenteral nutrition in critically ill patients with short-term relative contraindications to early enteral nutrition: a randomized controlled trial**. *Jama* 2013, **309**(20):2130-2138.
51. Meert KL, Daphtary KM, Metheny NA: **Gastric vs small-bowel feeding in critically ill children receiving mechanical ventilation: a randomized controlled trial**. *Chest* 2004, **126**(3):872-878.
52. de Betue CT, van Steenselen WN, Hulst JM, Olieman JF, Augustus M, Mohd Din SH, Verbruggen SC, Tibboel D, Joosten KF: **Achieving energy goals at day 4 after admission in critically ill children; predictive for outcome?** *Clin Nutr* 2014.
53. Sheridan RL, Yu YM, Prelack K, Young VR, Burke JF, Tompkins RG: **Maximal parenteral glucose oxidation in hypermetabolic young children: a stable isotope study**. *JPEN J Parenter Enteral Nutr* 1998, **22**(4):212-216.
54. Faustino EV, Hirshberg EL, Bogue CW: **Hypoglycemia in critically ill children**. *J Diabetes Sci Technol* 2012, **6**(1):48-57.
55. Hirshberg E, Lacroix J, Sward K, Willson D, Morris AH: **Blood glucose control in critically ill adults and children: a survey on stated practice**. *Chest* 2008, **133**(6):1328-1335.
56. Preissig CM, Rigby MR: **A disparity between physician attitudes and practice regarding hyperglycemia in pediatric intensive care units in the United States: a survey on actual practice habits**. *Crit Care* 2010, **14**(1):R11.
57. Vlasselaers D: **Blood glucose control in the intensive care unit: discrepancy between belief and practice**. *Crit Care* 2010, **14**(3):145.
58. Macrae D, Grieve R, Allen E, Sadique Z, Morris K, Pappachan J, Parslow R, Tasker RC, Elbourne D, Investigators CH: **A randomized trial of hyperglycemic control in pediatric intensive care**. *N Engl J Med* 2014, **370**(2):107-118.
59. Boonen E, Van den Berghe G: **Endocrine responses to critical illness: novel insights and therapeutic implications**. *J Clin Endocrinol Metab* 2014, **99**(5):1569-1582.

Figure legends

Figure 1. Participating countries (in grey).

Figure 2. Caloric intake in different age categories in the point-prevalence; $p < 0.001$ when comparing intake in the 3 different age categories (Kruskal-Wallis test)

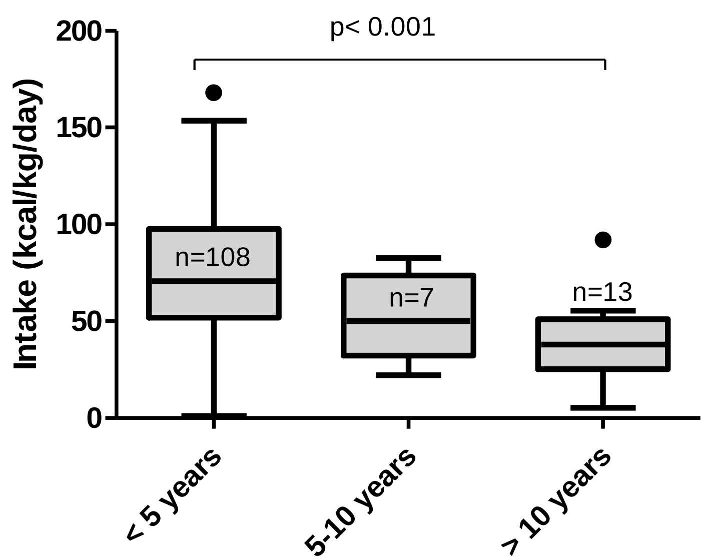


Figure 3. Early initiation of enteral and parenteral nutrition.

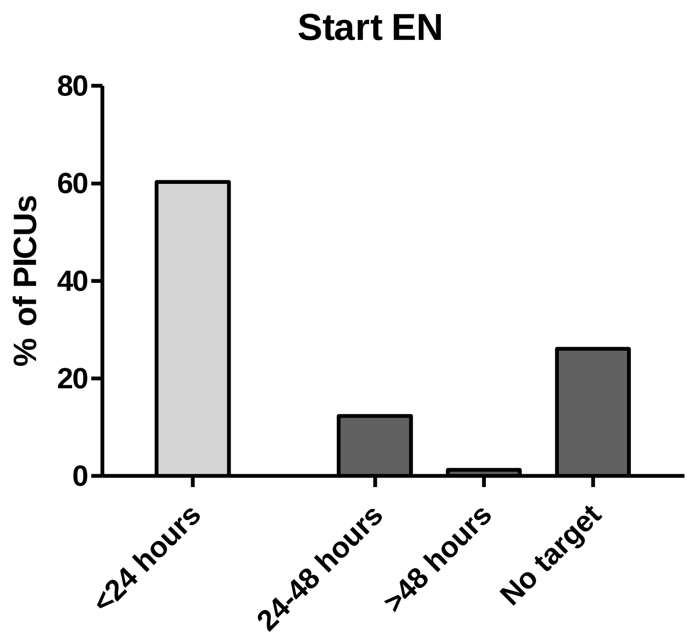
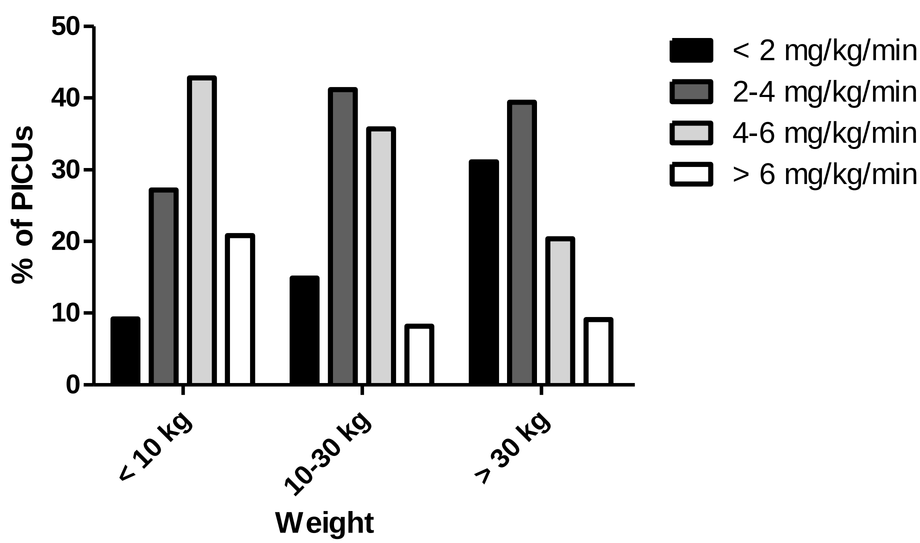


Figure 4. Varying target glucose intake in the first 24 hours of admission.



Tables

Table 1. PICU characteristics of the first (n=156) and point-prevalence part (n=42) of the survey

Characteristic	Number of PICUs (%)	
	Part 1: survey N=156	Part 2: point-prevalence N=42
Continent		
Asia	37 (24%)	9 (21%)
Africa	5 (3.2%)	2 (4.8%)
Europe	48 (31%)	17 (41%)
North-America	33 (21%)	3 (7.1%)
Oceania	9 (5.8%)	2 (4.8%)
South-America	24 (15%)	9 (21%)
Income category (country)		
Low	1 (0.6%)	0 (0.0%)
Lower middle	20 (13%)	2 (4.8%)
Upper middle	49 (31%)	15 (36%)
High	86 (55%)	25 (60%)
Hospital type		
General hospital	31 (20%)	7 (17%)
University hospital	51 (33%)	15 (36%)
Children's hospital	20 (13%)	4 (9.5%)
University-children's hospital	48 (31%)	14 (33%)
Type of PICU		
Multidisciplinary/mixed	135 (86%)	36 (86%)
Cardiac	6 (4.0%)	2 (4.8%)
Medical	8 (5.1%)	2 (4.8%)
Combination of PICU		
With adult ICU	9 (5.8%)	1 (2.4%)
With Neonatal ICU	25 (16%)	8 (19%)
With adult and neonatal ICU	3 (2.0%)	0 (0.0%)
Not combined	119 (76%)	33 (79%)
Size of PICU		
1-10 beds	76 (49%)	20 (48%)
11-20 beds	51 (33%)	14 (33%)
21-30 beds	23 (15%)	7 (17%)
>30 beds	6 (3.5%)	1 (2.4%)

Ventilated patients		
< 25%	22 (14%)	5 (12%)
25-50%	55 (35%)	13 (31%)
50-75%	49 (31%)	14 (33%)
>75%	30 (19%)	10 (24%)

Table 2. Characteristics of nutritional protocols

Characteristic	**Number of PICUs (%)** Total 156
Protocol available	82 (52%)
Information in protocol	
Assessment of energy requirements	72 (89%)
Protein requirements	65 (81%)
Management of GRV	57 (71%)
Type of EN	72 (89%)
Amount of EN	75 (94%)
Composition of PN	71 (88%)
Amount of PN	72 (89%)
Protocol age/weight differentiated	
Not	6 (7.7%)
For EN	8 (10%)
For PN	7 (8.7%)
For both EN and PN	59 (74%)

GRV: gastric residual volume; EN: enteral nutrition; PN: parenteral nutrition

Table 3. Parenteral lipid emulsions used in the PICU (more than 1 answer possible per PICU).

Lipids by brand	**Type**	**Number of PICUs (%)**
Intralipid	100% soy based	101 (65%)
SMOFlipid	30% soy, 25% olive oil, 15% fish oil, 30% MCT	44 (28%)
Omegaven	100% fish oil	16 (10%)
Clinoleic	80% olive oil, 20% soy	27 (18%)
Lipoplus	10% fish oil, 40% soy, 50% MCT	5 (2.9%)
Lipofundin	100% soy based	4 (2.2%)

Table 4.Overview of nutritional recommendations by A.S.P.E.N. and ESPEN/ESPGHAN and clinical practice.

Element	A.S.P.E.N. (2009 [11])	ESPEN/ESPGHAN (2005 [12])	Our survey
Target group	Nutrition in critically ill children	Parenteral nutrition in children Special sections for critically ill children	Nutrition in critically ill children
Nutrition assessment	Screening to identify (risk of) malnutrition	Regular measurements of height, weight and head circumference (<3 years). Skin fold thickness and mid arm circumference reflect body fat and protein. Biochemical measurements are not ideal	Nutritional status administered on admission and during stay, mostly by weight (94%), height (50%) and biochemical measurements (60%).
Nutritional protocols/support	Support team and protocols may enhance delivery of nutrition, no effect on outcome.	A NST should monitor the process of parenteral nutrition	Nutritional support team (56.8%) and protocol (52.4%) available to most PICUs, no effect on caloric intake or % EN.
Energy requirements	EE assessed throughout course of illness. Standard equations often unreliable for estimate of EE. IC desirable in subgroup of patients, if not available, energy provision based on formulas without correction factors.	Reasonable values for EE from prediction equations without stress factors. Measurement of REE may be useful in the individual patient.	Standard equations commonly used; in 70% of PICUs in combination with correction factors, as fever (41%), diagnosis (54%) and growth (59%). IC available in 14% of PICUs.
Timing of nutrition	No recommendations. Current practice is initiation of EN in 48-72 hours.	Time of initiation of PN will depend on individual circumstances and age and size of the child. Inadequate nutrition up to 7 days may be tolerated in older children.	Early initiation of EN and PN. Supplementation of inadequate EN with PN in majority of PICUs. Reaching nutritional targets by EN remains challenging.
Macronutrient intake	Insufficient data at moment of publication to make	Only parenteral recommendations	

	evidence-based recommendation		
Glucose		Glucose intake in critically ill children limited to 5 mg/kg/min	Varying glucose targets, mostly 2-6 mg/kg/min Median glucose intake first 24 hours 1.7 mg/kg/min
Protein	0-2 years: 2-3 g/kg/day 2-13 years: 1.5-2 g/kg/day 13-18 years: 1.5 g/kg/day	Neonates: 1.5-3 g/kg/day 2 months-3 years: 1.5-2 g/kg/day 3-18 years: 1-2 g/kg/day Critically ill children (3-12 years old): 3 g/kg/day amino acids	Varying protein targets, 66% not meeting target
Lipids (iv)	Most centers start at 1 g/kg/day and advance over a period of days to 2-4 g/kg/day with monitoring of TG levels	All children: infants max. 3-4 g/kg/day lipids, older children 2-3 g/kg/day. In PICU: more frequent monitoring and adjustment to TG concentration	Lipid target predominantly 1.5-2.5 g/kg/day, adjusted to TG concentration
Route of nutrition	EN preferred, if tolerated. PN if EN in insufficient. Insufficient data to recommend appropriate site. Gastric route is preferred, post-pyloric may be indicated to improve caloric intake or in children at high risk of aspiration or intolerant to gastric feeds	No recommendations on EN	EN preferred. PN if EN is insufficient. Gastric route is preferred in ventilated (67%) and non-ventilated (88%) patients. Prokinetics are used if a patient is not tolerating feeds.
Immunonutrition	Not recommended based on available literature at moment of publication	Not recommended based on available literature at moment of publication	No data

PICU: pediatric intensive care unit; NST: nutritional support team; EN: enteral nutrition; PN: parenteral nutrition; REE: resting energy expenditure; TG: triglycerides; IC: indirect calorimetry

582 Supplement: Table 1. Adjusted Odds ratios per continent.

PICU variable	OR (95% CI)	p
Nutritional protocol		
Asia	3.96 (1.53-10.25)	0.005
Africa	+∞	*
North-America	3.96 (1.35-11.66)	0.013
South-America	0.95 (0.33-2.76)	0.92
Oceania	0.87 (0.25-3.06)	0.83
Europe (reference)		
Nutritional support team		
Asia	1.2 (0.51-2.83)	0.68
Africa	+∞	*
North-America	0.32 (0.13-0.79)	0.14
South-America	0.17 (0.05-0.59)	0.005
Oceania	0.11 (0.02-0.62)	0.013
Europe (reference)		
Protein target by A.S.P.E.N.		
Asia	0.7 (0.27-1.81)	0.46
Africa	+∞	*
North-America	0.31 (0.12-0.76)	0.01
South-America	0.72 (0.24-2.17)	0.56
Oceania	1.05 (0.32-3.47)	0.94
Europe (reference)		
Protein target by ESPEN/ESPGHAN		
Asia	3.00 (1.29-6.99)	0.011
Africa	+∞	*
North-America	15.6 (4.18-58.28)	<0.001
South-America	1.3 (0.53-3.22)	0.57
Oceania	6.4 (1.06-38.84)	0.044
Europe (reference)		
Start of enteral nutrition		
Asia	1.31 (0.50-3.46)	0.58
Africa	+∞	*
North-America	2.08 (0.79-5.49)	0.14
South-America	1.19 (0.42-3.38)	0.74
Oceania	0.17 (0.04-0.67)	0.012
Europe (reference)		
Start of parenteral nutrition		
Asia	3.43 (1.43-8.22)	0.06
Africa	+∞	*

North-America	3.10 (1.53-6.29)	0.002
South-America	0.92 (0.36-2.35)	0.85
Oceania	1.50 (0.56-4.01)	0.42
Europe (reference)		
Glucose intake children < 10 kg		
Asia	0.64 (0.19-1.1)	0.087
Africa	+∞	*
North-America	0.44 (0.21-0.92)	0.029
South-America	0.73 (0.29-1.87)	0.507
Oceania	0.40 (0.14-1,14)	0.085
Europe (reference)		

OR: Odds ratio

*****Because the estimated odds ratio converged to 0 or infinity, Wald confidence intervals and p-values could not be calculated